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Carboxylative Cyclization of Propargylic Amines with Carbon Dioxide Catalyzed by Poly(amidoamine)-Dendrimer-Encapsulated Gold Nanoparticles

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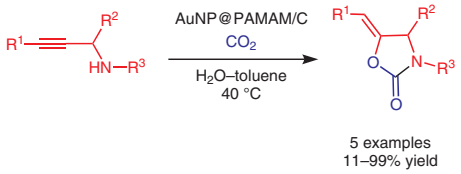

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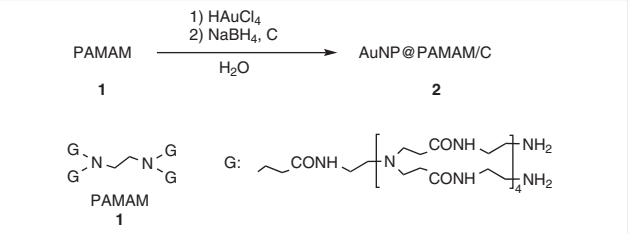
Abstract We prepared gold nanoparticles encapsulated in poly(amidoamine) (PAMAM) dendrimers as templating agents. The resulting gold nanoparticles were used as catalysts for the carboxylative cyclization of propargylic amines with carbon dioxide to afford the corresponding 1,3-oxazolidin-2-ones in yields of up to 99%.

Key words oxazolidinones, propargylic amines, carbon dioxide, gold catalysis, nanoparticles

The capture, fixation, and utilization of carbon dioxide (CO_2) have become important scientific and technological objectives because CO_2 is nontoxic, nonflammable, abundant, and easily available.[1] Moreover, CO_2 is one of the most attractive C_1 building blocks for replacing such toxic reagents as phosgene and carbon monoxide.[2] However, in the case of chemical transformations of CO_2, high pressures of CO_2 and high reaction temperatures are required because of the thermodynamic stability and kinetic inertness of CO_2. Nevertheless, many transformations of CO_2 have been studied with the aim of achieving sustainable development and green syntheses. One of the useful transformations of CO_2 is the carboxylative cyclization of propargylic amines with CO_2 to give 1,3-oxazolidin-2-ones.[3,4] Recently, various investigations of this reaction catalyzed by organometallic complexes of various transition metals such as ruthenium,[5] palladium,[6] silver,[7] and gold[8] have been conducted.

Metal nanoparticles have great potential in the field of catalysis.[9] The large surface area of metal nanoparticles promotes their catalytic activity, resulting in rapid chemical transformations with excellent product yields. Recently, gold nanoparticles have been reported to act as efficient catalysts for the cycloisomerization of 2-alkynylanilines to give indole derivatives.[10] This transformation was attributed to the formation of alkenyl gold intermediates derived from the triple bonds of the alkynes.[10b,11] In addition, monodisperse gold nanoparticles have been reported to be readily prepared by the use of poly(amidoamine) (PAMAM) dendrimers as templates.[12] Here, we report a carboxylative cyclization of propargylic amines with CO_2 to provide 1,3-oxazolidin-2-ones that is catalyzed by PAMAM-dendrimer-encapsulated gold nanoparticles.[13] In our screening of the preparation method for the dendrimer-encapsulated gold nanoparticles as catalysts, the addition of mesoporous carbon powder to the prepared gold nanoparticles mixture was found to be effective in promoting the carboxylative cyclization of propargylic amines with CO_2.

Gold nanoparticles were prepared within the fourth generation-PAMAM dendrimer (PAMAM **1**) by a modification of a previously reported synthetic sequence (Scheme 1).[12b] First, an aqueous solution of hydrogen tetrachloroaurate(III) was added to an aqueous solution of dendrimer **1** under argon. The resulting mixture was vigorously stirred for one hour to load the tetrachloroaurate(III) ion into the dendrimer. Next, the tetrachloroaurate(III) ions were reduced to form PAMAM-encapsulated gold nanoparticles (AuNP@PAMAM) by the addition of aqueous sodium tetrahydroborate to the mixture. Immediately after the reduction, mesoporous carbon powder was added to the reaction



Scheme 1 Preparation of the carbon-supported PAMAM-encapsulated gold nanoparticles **2**

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mixture to support the AuNP@PAMAM and to prevent aggregation of the gold nanoparticles.[14] Thirty minutes after the addition of the mesoporous carbon, the carbon-supported PAMAM-encapsulated gold nanoparticles **2** were obtained as an aqueous dispersion.

Scanning transmission electron microscopy (STEM) observation of **2** revealed the presence of spherical particles of 1–2 nm in diameter as the major component, indicating the formation of gold nanoparticles (Figure 1).[15]

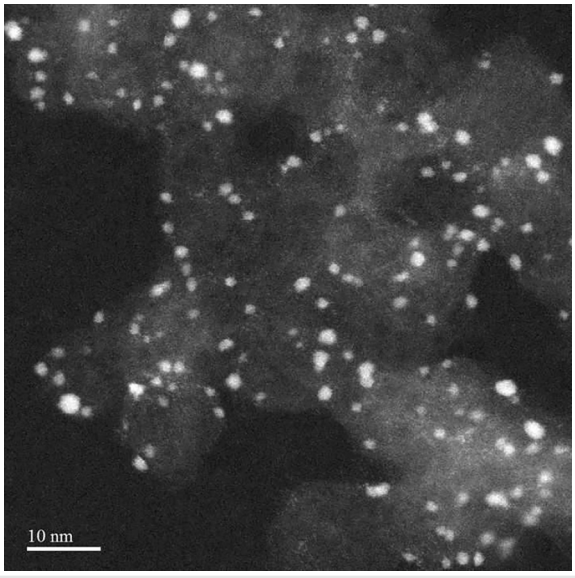
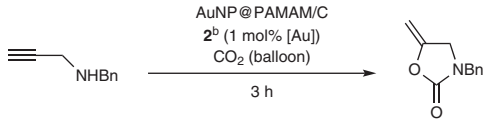


Figure 1 STEM image of gold nanoparticles **2**

Next, the prepared gold nanoparticles **2** were used directly as a catalyst for the carboxylative cyclization of propargylic amine **3a** with CO_2 (Table 1). CO_2 at atmospheric pressure (balloon) was used to displace the argon in the reaction vessel then amine **3a** was added to the aqueous dispersion of **2** and the mixture was stirred vigorously at 40 °C for three hours. The aqueous-phase carboxylative cyclization of propargylic amine **3a** with CO_2 proceeded smoothly in the presence of 1 mol% of gold nanoparticles **2** as a catalyst to give 1,3-oxazolidin-2-one **4a** in a 79% yield (Table 1, entry 1). Encouraged by this result, we carried out the carboxylative cyclization of **3a** in a water–toluene mixture, and the yield of **4a** increased to 96% (Table 1, entry 2). Then, the carboxylative cyclizations of **3a** were performed at various temperatures in a water–toluene solvent system (Table 1, entries 2–4), and 1,3-oxazolidin-2-one **4a** were obtained in good chemical yields (>90%), even at room temperature (Table 1, entry 3).

Next, to optimize the preparation method for the PAMAM-encapsulated gold nanoparticles **2** as a catalyst, we prepared **2** with various $HAuCl_4$/PAMAM ratios, and we used the resulting samples of **2** (1 mol%) as catalysts for the carboxylative cyclization of propargylic amine **3a** in a water–toluene at 40 °C for 15 minutes under CO_2 at atmospheric pressure. When **2** was prepared from $HAuCl_4$ and PAMAM in a ratio of 20:1, the 1,3-oxazolidin-2-one **4a** was obtained in moderate yield (62%; Table 2, entry 2).

Table 1 Carboxylative Cyclization of Propargylic Amine **3a** with CO_2 under Various Reaction Conditions[a]

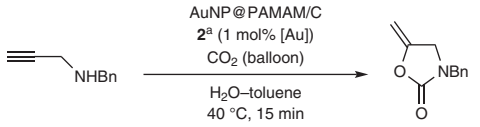


3a **4a**

Entry	Solvent	Temp (°C)	Yield[c] (%)
1	H_2O	40	79
2	H_2O–toluene	40	96
3	H_2O–toluene	r.t.	90
4	H_2O–toluene	60	94

[a] Reaction conditions: **3a** (1 equiv), **2** (1 mol% [Au]), H_2O (0.1 M based on **3a**; entry 1) or 2:1 (v/v) H_2O–toluene (0.067 M based on **3a**; entries 2–4), 3 h, CO_2 (1 atm).
[b] **2**: $HAuCl_4$/PAMAM = 20:1 (mol/mol), C/[Au] = 100:1 (w/w).
[c] Determined by integration of ^1H NMR absorptions with reference to an internal standard.

Table 2 Optimization of the $HAuCl_4$/PAMAM ratio for the Preparation of **2**



3a **4a**

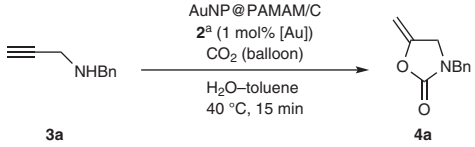
Entry[b]	$HAuCl_4$/PAMAM	Yield[c] (%)
1	10	50
2	20	62
3	30	50

[a] **2**: C/[Au] = 100:1 (w/w).
[b] Reaction conditions: **3a** (1 equiv), **2** (1 mol% [Au]), 2:1 (v/v) H_2O–toluene (0.067 M based on **3a**), 40 °C, 15 min, CO_2 (1 atm).
[c] Determined by integration of ^1H NMR absorptions with reference to an internal standard.

We subsequently optimized the amount of the mesoporous carbon powder in the preparation of the PAMAM-encapsulated gold nanoparticles **2** (Table 3). The carboxylative cyclization of propargylic amine **3a** with CO_2 was carried out for 15 minutes in the presence of 1 mol% of **2**, prepared with various C/[Au] (w/w) ratios, as a catalyst.[16] When the C/[Au] ratio was 50:1 or 30:1, the 1,3-oxazolidin-2-one **4a** was obtained in fair yields (85% and 82%, respectively; Table 3, entries 2 and 3).[17] In addition, it is noteworthy that the yield of 1,3-oxazolidin-2-one **4a** decreased markedly to 46% when no mesoporous carbon powder was used (entry 4). This confirmed the importance of meso-

porous carbon as a support. The use of mesoporous carbon to support the prepared gold-nanoparticles-containing PAMAM probably enhances the stability of the gold nanoparticles by suppressing their aggregation.[18]

Table 3 Optimization of the Amount of Mesoporous Carbon Powder for the Preparation of **2**



Entry[b]	C/[Au] (w/w)	Yield[c] (%)
1	100	62
2	50	85
3	30	82
4	0	46

[a] **2**: $HAuCl_4$/PAMAM = 20:1 (mol/mol).
[b] Reaction conditions: **3a** (1 equiv), **2** (1 mol% [Au]), 2:1 (v/v) H_2O–toluene (0.067 M based on **3a**), 40 °C, 15 min, CO_2 (1 atm).
[c] Determined by integration of ^1H NMR absorptions with reference to an internal standard.

The time-course curve of the carboxylative cyclization of a propargylic amine **3a** under the optimal conditions (Table 3, entry 2) is shown in Figure 2. The reaction was so fast that the chemical yield of the 1,3-oxazolidin-2-one **4a** reached 99% within half an hour.

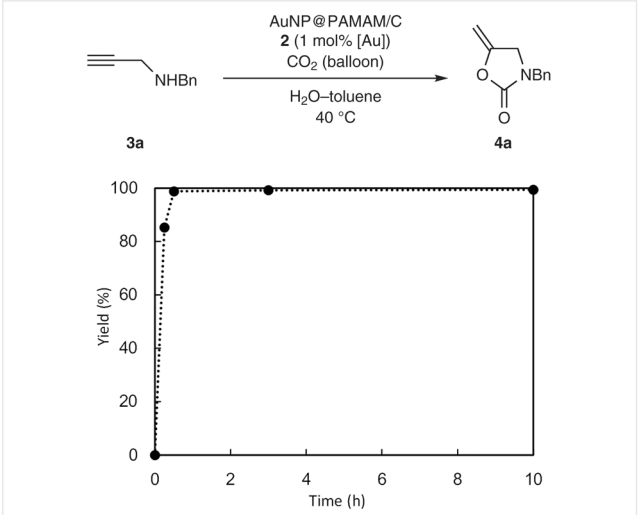
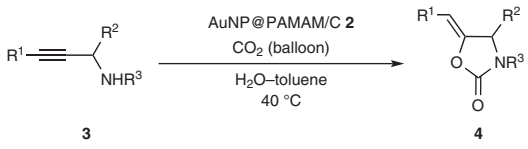
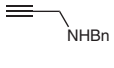
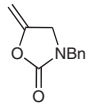
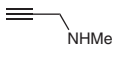
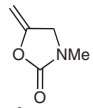
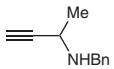
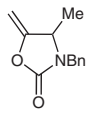
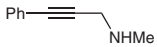
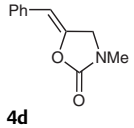
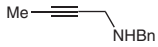
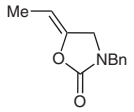
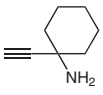
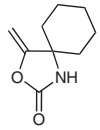


Figure 2 Time-course curve of the carboxylative cyclization of a propargylic amine **3a**

Finally, we performed the carboxylative cyclization of various propargylic amines **3** at 40 °C under CO_2 at atmospheric pressure in the presence of **2** as a catalyst (Table 4).[19] When *N*-benzylpropargylic amine (**3a**) and *N*-methylpropargylic amine (**3b**) were used as substrates for carboxylative cyclization in the presence of 1 mol% of **2** as catalyst, the corresponding 1,3-oxazolidin-2-ones **4a** and **4b** were obtained in yields of 99 and 89%, respectively (Table 4, entries 1 and 2). In contrast, the presence of an α-methyl group in **3c** resulted in a poor yield of **4c** (32%), even when 2 mol% of **2** was employed as a catalyst (entry 3). On the other hand, the presence of a terminal phenyl group in **3d** resulted in a moderate yield (76%) of **4d** (entry 4), whereas

Table 4 Carboxylative Cyclization of Various Propargylic Amines **3** for the Synthesis of **4**[a]



Entry	Substrate	Product	**2**[b] (mol% [Au])	Time (h)	Yield[c] (%)
1	 **3a**	 **4a**	1	10	99 (99)[d]
2	 **3b**	 **4b**	1	24	89 (87)[d]
3	 **3c**	 **4c**	2	24	32
4	 **3d**	 **4d**	2	24	76 (75)[d]
5	 **3e**	 **4e**	2	24	11
6	 **3f**	 **4f**	2	24	0

[a] Reaction conditions: 2:1 (v/v) H_2O–toluene [0.067 M based on **3a** and **3b** (entries 1 and 2), 0.033 M based on **3c–f** (entries 3–6)], 40 °C, CO_2 (1 atm).
[b] **2**: $HAuCl_4$/PAMAM = 20:1 (mol/mol), C/[Au] = 50:1 (w/w).
[c] Determined by integration of ^1H NMR absorptions with reference to an internal standard.
[d] Isolated yield.

the presence of a terminal methyl group in **3e** resulted in a low chemical yield (11%) of the corresponding 1,3-oxazolidin-2-one **4e** (entry 5).[20] Finally, when the primary amine **3f** was used as a substrate, the corresponding 1,3-oxazolidin-2-one **4f** was not obtained (entry 6).

Figure 3 shows our proposed mechanism for the carboxylative cyclization of propargylic amine **3** catalyzed by the PAMAM-encapsulated gold nanoparticles **2**. First, **3** reacts with CO_2 to form the corresponding carbamic acid **5** in situ.[8g] Carbamic acid **5** is activated by gold nanoparticle-π interactions of the triple bond and also by interaction of the hydrogen atom of **5** with a tertiary amine moiety of the PAMAM, as shown in structure **6**.[4c] The corresponding 1,3-oxazolidin-2-one **4** is then formed, with the regeneration of **2**.

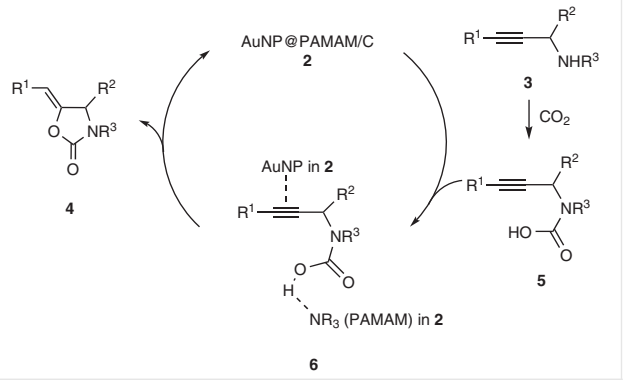


Figure 3 Proposed mechanism for the carboxylative cyclization of a propargylic amine **3** catalyzed by the PAMAM-encapsulated gold nanoparticles **2**

In summary, by employing the PAMAM-dendrimer-encapsulated gold nanoparticles as a catalyst, the carboxylative cyclization of various propargylic amines proceeded under CO_2 at atmospheric pressure to afford the corresponding 1,3-oxazolidin-2-ones. Gold nanoparticles of diameter 1–2 nm were successfully prepared within the PAMAM dendrimers. In addition, we found that the catalytic activity of the PAMAM-dendrimer-encapsulated gold nanoparticles increased markedly by addition of mesoporous carbon powder. Studies on further applications of this catalyst to other reactions are ongoing.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690162.

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(15) **2**: $HAuCl_4$/PAMAM = 20:1 (mol/mol), C/[Au] = 50:1 (w/w). A histogram showing the particle-size distribution of the gold nanoparticles **2** is given in the Supporting Information.

(16) [Au]: weight of gold in hydrogen tetrachloroaurate(III).

(17) In all cases in which **2** was prepared without hydrogen tetrachloroaurate(III) and/or PAMAM **1**, the carboxylative cyclization of **3a** with CO_2 did not proceed.

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(19) **1,3-Oxazolidin-2-ones 4a–e : General Procedure**
A reaction vessel was charged with 10% methanolic solution of the fourth-generation PAMAM **1** (21 mg, 0.15 μmol) under argon. The MeOH was removed in vacuo, and **1** was redissolved in H_2O (2.1 mL). A 0.005 M aqueous solution of $HAuCl_4$ (0.6 mL) was slowly added to the aqueous solution of **1** with stirring. The mixture was stirred for 1 h, then a 0.1 M solution of $NaBH_4$ in 0.3 M aq NaOH (0.3 mL) was added dropwise with vigorous stirring to reduce the $AuCl_4^-$ to Au nanoparticles. Immediately after the addition of the $NaBH_4$, mesoporous carbon powder (30 mg) was added, and the reaction mixture was vigorously stirred for 30 min to give the carbon-supported PAMAM-encapsulated gold nanoparticles **2** as an aqueous dispersion (3 mL in total), to which toluene (1.5 mL) was added with stirring. The atmosphere in the reaction vessel was then changed from argon to CO_2 and the mixture was heated at 40 °C. The appropriate propargylic amine **3** (0.3 mmol for Table 4, entries 1 and 2; 0.15 mmol for entries 3–6) was then added, and the mixture was vigorously stirred at 40 °C under CO_2 at atmospheric pressure for the appropriate time. Catalyst **2** was separated by filtration under a vacuum and washed with CH_2Cl_2. The filtrate was collected and extracted with CH_2Cl_2 (×4). The combined organic layer was dried (Na_2SO_4) and filtered, and the yield of the1,3-oxazolidin-2-one **4** was determined by integration of its ^1H NMR absorption with reference to an internal standard [2-(benzyloxy)naphthalene]. **4a**, **4b**, and **4d** were isolated by removal of the CH_2Cl_2 under reduced pressure and purified by column chromatography (silica gel, hexane–AcOEt).
3-Benzyl-5-methylidene-1,3-oxazolidin-2-one (4a)
yield: 57.4 mg (99%). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.30 (m, 3 H), 7.30–7.25 (m, 2 H), 4.74 (td, *J* = 2.6, 3.1 Hz, 1 H), 4.47 (s, 2 H), 4.24 (td, *J* = 2.2, 3.1 Hz, 1 H), 4.02 (t, *J* = 2.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 149.0, 135.0, 129.0, 128.25, 128.17, 86.7, 47.8, 47.2.

(20) In Figure 3, it is assumed that the nucleophilic ring closure from **6** to **4** is probably retarded when an electron-donating methyl group is present at R^1.